The Differential Diagnosis of Adult Rheumatic Fever and Rheumatoid Arthritis*

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THE differential diagnosis of rheumatic fever and rheumatoid arthritis is said to be easy. But this refers to textbook cases which do not always occur in practice. As a matter of fact, experience during the last war has stressed the difficulties encountered in the differentiation between these two diseases. The importance of carditis in the diagnosis of rheumatic fever[11] cannot be over-emphasized. However, it has been long recognized that in adult rheumatic fever signs of carditis may be entirely absent or of such a fleeting nature that they are overlooked. For example, of a series of 415 cases of adult rheumatic fever, definite carditis could not be demonstrated in 40 per cent, despite frequent electrocardiographic and other studies.[6] Failure to demonstrate carditis, then, may be one reason for diagnostic difficulties.

Rheumatoid arthritis with its prodromal constitutional symptoms, followed by an insidious onset and slow progression of joint manifestations is an easily recognized entity. But the type of rheumatoid arthritis causing the greatest diagnostic confusion does not fulfill the classic description. As many as 10 per cent of the patients admitted into army centers for rheumatic fever were later found to have chronic joint disease clinically similar to rheumatoid arthritis.

It is currently believed by most American workers[1,3,9] that these cases are examples of the acute, "atypical" form of rheumatoid arthritis. With its sudden onset this type of rheumatoid arthritis may be of varying severity and it may or may not be followed by a symptomatic remission. If observed long enough, these patients will usually show frequent recurrences or exacerbations and sooner or later will merge into the more characteristic clinical picture of rheumatoid arthritis. The development of chronic arthritis following an initial illness which simulates rheumatic fever is one reason for the opinion[4,7,8] that rheumatoid arthritis may be a residue of and secondary to rheumatic fever. However, the common pathogenesis of these two diseases has never been established. Nor is it likely that such a controversial concept can be definitely accepted or rejected until the etiology of both diseases is known. In the meantime we may regard these as separate entities and every effort should be made clinically to differentiate between them. The prognostic and therapeutic implications of early, accurate diagnosis are all too clear.

It would appear, then, that the problem at hand resolves itself into how one may distinguish between adult rheumatic fever without carditis and acute, atypical rheumatoid arthritis. It is this question that the following study has attempted to answer. A clinical comparison has been made of patients who, admitted into Army Service Forces rheumatic fever centers, were later discharged with a diagnosis of either rheumatic fever or rheumatoid arthritis. For this purpose the selected rheumatic fever patients have been limited to those with evidence of carditis, either permanent or transitory, and exclusive of the transient systolic murmur. For comparison only those cases of rheumatoid arthritis showing characteristic joint x-ray findings have been included. While these findings are not thought of as prerequisites for correct diagnosis, they are sound and objective diagnostic criteria upon which a comparative study such as this must be based. Two hundred fifty-two patients with rheumatic fever and with significant carditis, as defined above, have been compared with thirty-three soldiers, who, admitted with a diagnosis of rheumatic fever, were later considered to have atypical rheumatoid arthritis with diagnostic x-ray changes. All patients were observed for from six to fifteen months. Significant similarities and dissimilarities between these two groups are now presented.

AGE RANGE OF PATIENTS

The average age of the patients with rheumatoid arthritis was 28.4 years, some four years older than that of the rheumatic fever patients. However, the age range, as well as the distribution of sex and color, was the same in both groups. The youngest patient in either group was 18 years. The oldest rheumatoid was 39 years old, while the oldest individual with rheumatic fever, a dental officer in his initial attack, was 45 years of age. A history of at least one attack of previous polyarthritis was obtained in 40 per cent of the rheumatic fever patients and in 57 per cent of the rheumatoids. The available data concerning their past illness were in most cases insufficient for proper diagnostic appraisal.

An incident of some significance was the antecedent sore throat or upper respiratory infection. (Table 1.) Seventy-two per cent of the rheumatic fever patients gave such a history seven to twenty-eight days before the onset of joint symptoms, while only 9 per cent of the rheumatoids gave a similar

TABLE 1.—*Antecedent Upper Respiratory Infection in Adult Rheumatic Fever and "Atypical" Rheumatoid Arthritis*

	RF	RA
Antecedent URI	81%	24%
7 - 28 days before onset	72%	9%
Less than 7 days before onset	9%	15%
No antecedent URI	19%	76%

* Read before the California Heart Association at the 75th Annual Session of the California Medical Association, Los Angeles, May 7-10, 1946.

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history. Fifteen per cent of the rheumatoids complained of a preceding upper respiratory infection within three days or less, while 76 per cent denied any such event. Both the antecedent respiratory infection and its time relationship with the onset of articular symptoms are worthy of attention.

Two hundred four, or 81 per cent, of the patients with rheumatic fever and all of those eventually diagnosed as atypical rheumatoid arthritis showed objective evidence of joint disease, including intra- or peri-articular effusions. In both groups of cases the initial joint symptoms were most often referable to one of the weight-bearing articulations, usually the knee or ankle with subsequent symmetrical, polyarticular involvement. Contrary to what might have been expected, the polyarthritis of adult rheumatic fever was migratory in only 37 per cent of those patients on whom adequate data were available, whereas in the remaining 63 per cent the arthritis was of a progressive nature in that the symptoms and signs, in previously affected joints, persisted for the duration of the arthritis. Among the rheumatoids the arthritis was always progressive. The average duration for the development of the polyarthritis of rheumatic fever was 6.4 days, while among the rheumatoids the development was considerably slower, an average of 19.1 days. At the climax of the polyarthritis the distribution of joint affection was the same in both groups, with small joint involvement of the fingers and toes in approximately one-half of the patients.

The remarkable effect of salicylates in rheumatic fever has been long recognized.[12] In adult rheumatic fever, however, one must distinguish between the subjective joint response to salicylates and the objective response, specifically the rate at which joint swelling disappears. It was not unusual for rheumatic fever patients to continue to experience joint pains for several months despite adequate salicylates. But joint effusions usually disappeared in a few days, and never more than 18 days, provided the patient was properly treated. And although a recrudescence of frank arthritis was not uncommon when salicylates were prematurely discontinued during signs of active disease, such an exacerbation was not observed among the rheumatic fever patients while adequate salicylization was maintained. Among those with rheumatoid disease, 91 per cent continued to show joint swelling for five weeks to several months, and in many cases there occurred an exacerbation or a progression of frank arthritis despite intensive salicylate therapy.

JOINT DEFORMITIES IN RHEUMATOID PATIENTS

Residual joint deformities, manifested chiefly by periarticular thickening, usually in the wrist, knee or ankle were observed in 63 per cent of the rheumatoid patients. In none of the patients with rheumatic fever could definite, residual joint deformity be demonstrated. Transient limitation of joint function and local muscle atrophy were occasionally seen in rheumatic fever convalescents. These were probably due to improper mobilization and were easily corrected.

Chorea and subcutaneous nodules are frequently mentioned in differential diagnosis, although they are rarely found in adult rheumatic fever. However, nodules should be sought for and biopsied, especially in the event of a diagnostic problem. The histologic picture may determine the rheumatic or rheumatoid nature of the disease.[2] Nodules were recorded in two rheumatic fever patients, and in one rheumatoid. No case of chorea was observed in the presence of active carditis. Erythema in one or another of its many forms occurred in 7 per cent of the rheumatic fever group, while it was never observed in association with rheumatoid arthritis. The degree of fever, leukocytosis and/or anemia was not helpful in differential diagnosis. Signs of purpura, most commonly in the form of epistaxis, were observed in 22 per cent, while pulmonic changes occurred in association with rheumatic fever in 8 per cent of the cases. Only one patient with rheumatoid arthritis experienced spontaneous nose-bleeds, while neither pleurisy nor pneumonitis was ever observed.

A significant difference in the duration of the abnormally elevated sedimentation rates was noted. (Table2.) While the average period of high sedimentation rates was approximately ten weeks among the rheumatic fever patients and 25 weeks among the rheumatoids, this contrast was even more striking when broken down further. Of the rheumatic fever group, 33 per cent showed a normal sedimentation rate four weeks after the onset of the disease; 61 per cent were normal within eight weeks. Of the rheumatoids, only one showed a normal sedimentation rate at the end of the eighth week, and the majority continued to have a high rate for several months thereafter.

TABLE 2.—*Elevated Sedimentation Rates in Adult Rheumatic Fever and "Atypical" Rheumatoid Arthritis*

Duration	RF	RA
Average	9.9 weeks	25.3 weeks
Elevated 1 - 4 weeks	33%	0
Elevated 5 - 8 weeks	28%	3%
Elevated 9 - 12 weeks	16%	17%
Elevated 13 - 24 weeks	16%	37%
Elevated more than 24 weeks	7%	43%

It had been hoped that valuable aid in differential diagnosis might be derived from the antistreptolysin titer. The results were disappointing, chiefly because 60 per cent of the rheumatic fever group showed normal titers* while as many as 22 per cent of the rheumatoids were abnormally high. Elevated antistreptolysin titers in acute rheumatoid arthritis have been previously described.[5]

BONE AND JOINT X-RAYS

Bone and joint x-rays were normal among the rheumatic fever patients except for transient osteoporosis, which was observed in a few cases whose course had been marked by multiple recrudescences

* It should be noted that the initial titers were not obtained before the sixth week of the disease in most cases.

of arthritis. The rheumatoid changes consisted chiefly of demineralization and joint narrowing. In this connection, it is well to remember that joint x-rays in rheumatoid arthritis may be entirely normal for months to years following the onset of the disease. Of great interest was the discovery that 39 per cent of the cases of rheumatoid disease showed significant changes in the sacro-iliac joints indicative of early rheumatoid spondylitis or so-called Marie-Strumpel disease. It has been recently shown that the spinal fluid protein in this type of case is often elevated.[10] Spinal fluid examination was done in seven such patients, of whom five showed normal values and two showed a protein concentration of 80 and 99 mg. per cent respectively. Spinal punctures performed on ten patients with rheumatic fever failed to show any increase in the spinal fluid protein. In the presence of symptoms and signs of rheumatoid spondylitis, an elevated spinal fluid protein may verify such a diagnosis despite the absence of positive x-ray findings and thereby assist in differential diagnosis.

The importance of carditis in the differential diagnosis of rheumatic fever and rheumatoid arthritis has been mentioned. However, neither the absence nor presence of cardiac involvement should necessarily determine the final diagnosis. It has been previously pointed out that carditis in adult rheumatic fever is not demonstrable in a significant percentage of cases. Occasionally one encounters carditis in association with rheumatoid arthritis. Often the two diseases coexist, either in the combination of rheumatoid arthritis and superimposed active rheumatic fever, or rheumatoid arthritis and inactive rheumatic heart disease. The latter was believed to be the case in four of the patients showing x-ray signs of rheumatoid arthritis. The proper differential diagnostic appraisal of such patients must rely to a great degree on the bahavior of the arthritis, as well as other clinical features.

It is said that differentiation between rheumatic fever without carditis and rheumatoid arthritis may be impossible. However, this should apply chiefly to those cases in which the joint manifestations subside in a few days. In such examples of atypical rheumatoid arthritis one cannot make an early unequivocal diagnosis. This must await prolonged follow-up studies. But in many cases of atypical rheumatoid arthritis an early, positive diagnosis can be made. On the basis of observations already recorded in this paper, the differential points listed in Table 3 should be most helpful toward this end. The following features are emphasized:

1. Carditis, when present, usually indicates rheumatic fever although not necessarily so.

2. The arthritis of atypical rheumatoid disease is apt to be progressive and not migratory, while in adult rheumatic fever it may be either progressive or migratory.

3. The progression of the arthritis may be slower in rheumatoid disease than in rheumatic fever.

4. Unlike rheumatic fever, the antecedent upper respiratory infection is infrequent in rheumatoid arthritis, and when it does occur the latent period is usually significantly shorter.

5. The therapeutic ineffectiveness of salicylates and their failure to halt further progression characterizes their action in rheumatoid arthritis. In rheumatic fever, the objective joint improvement is dramatic with the proper administration of salicylates, which exert an equally effective prophylaxis against recrudescences of frank arthritis.

6. Erythema, purpura and signs of pulmonary or pleural involvement should favor the diagnosis of rheumatic fever.

7. The elevated sedimentation rate of rheumatoid arthritis continues for a prolonged period, while in most cases of rheumatic fever it is of comparatively short duration.

With these points in mind, many if not all of the atypical rheumatoid arthritis cases which were mistakenly admitted into rheumatic fever centers might have been correctly diagnosed within a few weeks or days, rather than months following the onset of the disease.

TABLE 3.—*Most Helpful Differential Diagnostic Features*

	Adult RF	"Atypical" RA
Carditis	Often present.	Usually absent.
Arthritis	Progressive or migratory, faster in its evolution; no objective residue.	Usually progressive, slower in its evolution; residue common.
Antecedent URI	Usually present with longer latent period.	Usually absent; shorter latent period.
Effect of Salicylates	Prompt improvement of objective joint findings; protects against joint recrudescences.	May be totally ineffective.
Erythema	Often present.	Not observed.
Purpura	Often present.	Rare.
Pleurisy	Often present.	Rare.
Pneumonitis	Often present.	Not observed.
Elevated Sed. Rate	Usually of shorter duration.	Usually over prolonged period.

SUMMARY AND CONCLUSIONS

1. A comparative study was made of 252 soldiers with active rheumatic fever with carditis and 33 soldiers with acute, "atypical" rheumatoid arthritis with diagnostic joint and x-ray changes.

2. The most helpful differential diagnostic features have been outlined.

3. It is concluded that accurate and relatively early differentiation between adult rheumatic fever with or without carditis and atypical rheumatoid arthritis can be accomplished in a significant number of cases.

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REFERENCES

1. Bauer, W.: The Diagnosis of the Various Arthritides, New England Journal of Medicine, 221:524 (Oct. 5), 1939.

2. Bennett, G. A., Zeller, J. W., and Bauer, W.: Subcutaneous Nodules of Rheumotoid Arthritis and Rheumatic Fever, Arch. of Path., 30:70 (July), 1940.

3. Comroe, B. I.: Arthritis, Philadelphia, Lea and Febiger, 1944.

4. Dawson, M. H.: Chronic Arthritis, Nelson's New Loose-Leaf Medicine, 605, 1935.

5. Dawson, M. H. and Olmstead, M.: Antistreptolysin Titers in Rheumatoid Arthritis, Proc. of Soc. for Exper. Biol. & Med., 34:82-84 (Feb.), 1936.

6. Engleman, E. P.: Adult Rheumatic Fever, Presented at American Rheumatism Association, New York City, June, 1946, to be published.

7. Fischer, A.: Rheumatismus and Grenzgebiete, Berlin, J. Springer, 1933.

8. Freund, E.: Gelenkerkrankungen, Berlin, Urban and Schwarzenberg, 1929.

9. Hench, P.: Chronic Arthritis, in Barr's Modern Medical Therapy in General Practice, 1940.

10. Ludwig, A. O., Short, C. L., and Bauer, W.: Rheumatoid Arthritis as a Cause of Increased Cerebrospinal-Fluid Protein, New England Journal of Medicine, 228:306 (March 11), 1943.

11. Master, A. M. and Jaffe, Harry: Rheumatoid Arthritis and Acute Rheumatic Fever—The Differential Diagnosis, J.A.M.A., 98:881 (March 12), 1932.

12. Swift, H. F.: Rheumatic Fever, American Journal of Medical Sciences, 170:631 (Nov.), 1925.

Public Measures for the Control of Rheumatic Fever in England

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DURING the 17th century rheumatism affecting the body and multiple joints was first distinguished from gout which had previously been confounded with it. In 1676 Thomas Sydenham gave the first full clinical description of acute rheumatism and said that it chiefly attacked young people. Some years later he also described chorea, which was for a long time called Sydenham's chorea. But it was not until about 1800 that it became recognized, thanks largely to David Pitcairn and Matthew Baillie, that rheumatism was a disease which commonly affected the heart. Then in France Corvisart in 1806 began to refer to carditis, and Bouillaud in 1835 to describe and stress the frequency of endocarditis in acute articular rheumatism. By 1845, a century ago, a big step was reached when Sir Thomas Watson could write in his textbook of Physic: "It is a curious circumstance that rheumatic carditis is sometimes the first step in the whole disease; the cardiac symptoms will sometimes, I mean, precede those of the joints; even by two or three days."

Towards the year 1890 the medical profession in England began to realize that in acute rheumatism (or rheumatic fever) the country was faced with a problem of great national importance as a common source of cardiac disease. The British Medical Association carried out a collective investigation not only into its clinical features but also into the distribution and social and environmental associations of the disease.

Cheadle, a London physician and pediatrician, published in 1889 his lectures entitled "The various manifestations of the rheumatic state," lectures in which he urged a wider view of rheumatism than that of a polyarthritis: that the carditis was the essential fact about it, and not the condition of the joints which might be minimal and was often overlooked. Public attention to the subject was drawn by Sir Arthur Newsholme who produced the first epidemiological survey, and by Sir George Newman with his report from the Ministry of Health—not forgetting the powerful appeals to the profession and to the authorities by Dr. F. J. Poynton. The first direct result of this aroused public opinion was the setting aside in 1926 by the London County Council (L.C.C.) of 60 beds at Carshalton to accommodate children under the age of 16 with rheumatic fever. At the same time the other features of a general scheme for controlling rheumatic fever among the children of London were initiated.

THE LONDON COUNTY COUNCIL RHEUMATIC SCHEME

It seems best to describe the London County Council Rheumatic Scheme of control as it was in operation in 1938-39, before the second world war broke out.

1. *The Source of the Rheumatic Cases:*

There was already in operation by the L.C.C. a system of regular medical examination of all school children by school medical officers whose function was almost entirely diagnostic, and they became especially interested in the recognition of rheumatic manifestations among the children routinely examined. Then, general practitioners who in their practice found a child suffering in this way, were invited to communicate with the central office or supervisory center if the parents were willing for the child to be moved to hospital. These supervisory centers, to be described later, were also the source of many cases, chiefly relapses, among those already under their regular supervision. Lastly, most general hospitals, as well as children's hospitals in and around London, were glad to free their beds of some children with rheumatic infection who needed longer hospital treatment than they could continue to give.

It became apparent that an intermediate examination by a medical referee was necessary between the application for admission to hospital and the

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